Breast and Cervical Cancer Control Program
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New Technologies in Pap Test Screening and Evaluation

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As everyone involved in women's health is aware, the cervical smear (Pap test) is a very effective tool in screening for squamous cell carcinoma of the cervix. In theory, the Pap test is an ideal screening tool for cervical cancer. Ideally, a screening procedure should be: non-invasive, have a small risk of side effects, be inexpensive, recognize a pre-cursor lesion for which there is good therapy to prevent invasive cancer and be sensitive to the presence of abnormalities. In practice, the incidence and mortality from cervical cancer have decreased over 40 percent since 1973. Even so, cervical cancer remains a very real health threat to women. In 1998, there were an estimated 13,700 new cases of cervical cancer and a woman's lifetime risk of developing cervical cancer during her lifetime is .83 percent. Most of these cases of cervical cancer were in women who had never had a Pap test, or who had not had one in the past five years.

Despite the successes of the Pap test, it is not a perfect test. Both false positive and false negative results occur and can result in the development of advanced disease or in over-treatment with increase in side effects and costs. A false negative Pap test occurs when there is an abnormality in the cervix and the Pap test is interpreted as negative. This can be the result of an error anywhere in the process of obtaining and interpreting the Pap test. The majority of false negative cases are the result of inadequate sampling of the lesion on the cervix. If the lesion is not sampled then no abnormal cells will be present on the Pap test and it will be interpreted as negative. A smaller percentage of false negatives result from laboratory error. Cytology error can be the result of failure to find a few abnormal cells (screening error) or the finding of abnormal cells and misinterpreting them as normal (diagnostic error).

Within the last 10 years there has been a flurry of research, development and subsequent aggressive marketing of a variety of new technologies aimed at improving the Pap test. The Agency for Health Care Policy and Research (AHCPR) has just completed an extensive study and meta-analysis of the available literature on these new technologies and published their results in February 1999. The two technologies that are believed to remain viable are computer assisted screening (AutoPap) and liquid-based technologies (ThinPrep and AutoCyte).

Automated Pap test screening is aimed at reducing the number of false negative tests that occur through laboratory errors. Primary automated screening utilizes the computer as a screening cytotech. All Pap tests are screened by the machine and a certain percentage of cases deemed "most normal" are filed. The remaining cases are screened by a cytotech. Automated quality control (QC) utilizes the computer as a QC tech. After all the cases are looked at by a cytotech, all cases found to be normal are rescreened by the machine. Those most likely to contain significant abnormalities are passed on for review by a QC tech. In both cases, the cytotechs are armed with information as to how abnormal the case is thought to be and where some of the abnormal cells are on the slide.

The advantages of automated screening are that it can be placed directly into a laboratory with only a small amount of training. There is also significant improvement in the detection of screening and diagnostic errors. The disadvantages are that this method does not address sampling errors that are the cause of the majority of false negative Pap tests. Additionally, the costs ($3-$5 per slide) greatly increase the cost of Pap test interpretation.

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The liquid-based technology is aimed at reducing sampling errors and limited tests and constitutes a radical change in the way Pap tests are obtained. With these systems, as with a conventional Pap test, a swab or brush is used to obtain material from the cervix. However, rather than being tested on a slide, the swab is placed into a container of fluid. This container is mailed to the laboratory where 10% of the cells are transferred as a single cell layer to a slide. This method eliminate air-drying artifact, problems with test thickness and obscuring blood or inflammation. The remaining material can be used for other tests (chlamydia, gonorrhea, HPV, etc).

The resulting test is far less likely to be limited or unsatisfactory than the conventional Pap test. The sensitivity of Pap test interpretation can be improved with a reduction in the false negative fraction of 60 percent. The first disadvantage is that laboratory personnel have to be retrained in interpretation of these new tests. The more significant disadvantage is cost. With a cost per slide of $9-$10 per Pap test, this technology can double or triple the cost of a laboratory to interpret a Pap test.

These technologies both increase the sensitivity of the Pap smear test, but at a significant cost. The AHCPR study investigated the cost/benefit of these new technologies. The findings of the study were the following:

1) The sensitivity of the conventional Pap test is significantly less than what is perceived and is about 51 percent.
2) At the estimated reduction in the false negative fraction of 60 percent, the costs of these new technologies outweigh the benefits for annual Pap tests.
3) However, for patients who have extended screening intervals at every 3 years, the benefits of these new technologies outweigh the costs.

With these findings in mind, BCCCP is developing a process to obtain approval to reimburse these new technologies. For women receiving annual Pap tests, these new technologies will be reimbursed at the same rate as the conventional Pap test. For women who are receiving a Pap every three years or women who have never been screened before, the reimbursement for liquid-based Pap tests will be at the Medicare higher rate. This requires Centers for Disease Control and Prevention approval.

References:
Agency for Health Care Policy and Research, "Evaluation of Cervical Cytology" Feb 1999. Available at **www.ahcpr.gov**

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Critical Commentary: Invest Health Resources in Widespread Pap Screening, Not New Technologies

WASHINGTON, DC -- New cervical cancer screening technologies are not likely to help women most in need of cervical cancer testing and could even widen the economic gap between women who get Pap smears and those who don't, argue commentators in the August issue of Obstetrics & Gynecology. Health care resources would be better invested in a comprehensive national screening program that targets women most at risk for cervical cancer -- low-income women who never get tested at all -- rather than in refinement of testing techniques for women who already get Pap smears.

The greatest problem in cervical cancer screening in the United States is not the need for a better screening test, but the inability to provide cervical smears for highest-risk women, argue obstetrician-gynecologists George F. Sawaya, MD, of the University of California, San Francisco, and David A. Grimes, MD, of the University of North Carolina School of Medicine. Women who are not getting Pap smears tend to be older, uninsured, minorities, poor, and living in rural areas. They are disproportionately represented among the 4,900 U.S. women who die from cervical cancer each year: many of these deaths could be prevented if women had access to current Pap technology.

While improving the validity of Pap technology is important, the commentators add, some of the new and more expensive screening techniques appear to be driven "by perceived consumer need." They confer relatively small benefits to women most likely to be at low risk: women who can afford and have access to periodic Pap testing. By far the greater need, say Sawaya and Grimes, is "a comprehensive national screening program that targets women at highest risk. New screening technologies do not address the current utilization gap and might widen it by driving the costs of screening out of the reach of high-risk women."

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